C3 26. (new) The method of claim 1 wherein the DNA polymerase is thermal-stable.

REMARKS

Applicants have amended claims 1 and 25 and added new claim 26. Support for the amendments to claim 1 is found throughout the application and are particularly found at page 3, lines 25-29 and page 14, lines 8-14. Support for new claim 26 is found throughout the specification and particularly at page 5, lines 29-31.

Specifically, claim 1 recites that a method for the amplification of a population of nucleic acids wherein a four-enzyme mix comprising a DNA polymerase is used to synthesize double-stranded DNA. Claim 25 which is dependent on claim 1 has been amended to reflect the amendments to claim 1. New claim 26 is dependent on claim 1 and recites the further limitation that the DNA polymerase of claim 1 is thermal-stable.

Applicants respectfully request reconsideration of the pending rejections and reexamination of the present claims in light of the amendments and the remarks detailed below. It is submitted that no new matter has been introduced by the present amendments and entry of the same is respectfully requested.

By these amendments, the Applicants do not acquiesce to the propriety of any of the Examiner's rejections and do not disclaim any subject matter to which the Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997); *and Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 56 U.S.P.Q.2d 1865 (Fed. Cir. 2000).

Support for new claim 26 is found in the specification, for example, at page 5, lines 30-31.

Non-statutory Double Patenting

The Examiner has maintained the provisional obviousness-type double patenting rejection of claims 5-8 and 10-22, over claims 1-17, 24-43, and 50-69 of copending Application Ser. No. 09/285,658. See, paper No. 17 at pages 2-3, paragraph 3. Applicants respectfully traverse this rejection. Without acquiescing to the rejections, and because these rejections are provisional, Applicants respectfully request that the rejections be held in abeyance until a patent may issue from copending Application Ser. No. 09/285,658.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1, 3-13 and 20-25 are rejected under 35 U.S.C. §112, second paragraph. See, paper No. 17 at page 3, paragraph 5. Specifically, the Examiner asserts that it is unclear how the language "said amplification is proportional" is defined in the specification. *Id.*

Applicant's have amended claim 1 to remove the language "said amplification is proportional" and to more specifically point out the currently claimed invention. Applicants have added the limitation that a four-enzyme mix is added to synthesize the double-stranded DNA and that one of the four enzymes is a DNA polymerase. Support for this amendment can be found in the specification, for example, in Example 1, specifically page 14 lines 9-14.

Anticipation Rejection Under 35 U.S.C. §102(b)

The Examiner rejected claims 1, 3-7 and 22-25 under 35 U.S.C. §102(b) over Sooknanan *et al.* (WO 96/17079). See, paper No. 17 at page 7, paragraph 4. Applicants respectfully traverse this rejection.

In order to support anticipation under 35 U.S.C. § 102(b), each and every element of a claimed invention must be disclosed within a single prior art reference. *See In re Bond,* 15 USPQ2d 1896 (Fed. Cir. 1991) and *Scripps Clinic & Research Found. v. Genentech Inc.,* 927 F.2d 1565, 1576 (Fed. Cir. 1991).

As claimed, the current invention relates to a method for amplification of a population of nucleic acids wherein a four-enzyme mix comprising a DNA polymerase is used to synthesize double-stranded DNA from a population of single-stranded DNA.

Sooknanan *et al.* teaches a method for amplifying a specific nucleic acid sequence or its complement and further requires the presence of a terminal repeat in the template. When copied into the 3' end of the first strand cDNA the terminal repeat forms a hairpin that is used to prime synthesis of the second strand cDNA. Sooknanan *et al.* does not teach or disclose the amplification of a nucleic acid population and, in fact, teaches away from amplification of a population of nucleic acids, such as total cellular RNA, because the method requires all sequences to be amplified to have a terminal repeat. In addition, Sooknanan *et al.* teaches the use of a single enzyme with both RNA and DNA dependent DNA polymerase activities for synthesis of double-stranded DNA from a population of RNA. In the current invention a four-enzyme mix comprising a DNA dependent DNA polymerase is added to single-stranded DNA to synthesize double stranded DNA. Because these limitation of the instant claims are absent from Sooknanan *et al.*, this reference does not anticipate the instant claims 1, 3-7, and

22-25. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Obviousness Rejection Under 35 U.S.C. §103 - Sooknanan et al. in view of Kwoh et al. and Goller et al.

Claims 8-13 were rejected under 35 U.S.C. 103(a) over Sooknanan *et al.* as applied to claims 1 and 3-7 of the instant claims, and further in view of Kwoh *et al.* (86 PROC. NATL. ACAD. SCI. USA 1173-77 (1989)) and Goller *et al.* (16 ONCOGENE 2945-48 (1998)). Applicants respectfully traverse this rejection.

As set forth above, Sooknanan *et al.* does not disclose the limitation of independent claim 1 that a population of nucleic acids is amplified or the limitation that double-stranded DNA is synthesized from single-stranded DNA by the addition of a four-enzyme mix containing a DNA polymerase.

Kwoh *et al.* and Goller *et al.* do not remedy the deficiencies of Sooknanan *et al.* Like Sooknanan *et al.*, Kwoh *et al.* teaches the amplification of a specific sequence and not amplification of a population of nucleic acid sequences. Kwoh *et al.* also teaches the use of a single enzyme for synthesis of both first and second-strand cDNA. Unlike the current invention, no additional enzymes are added to accomplish second-strand cDNA synthesis.

Goller *et al.* teaches a method for identification of differentially expressed mRNA that requires purification of the double-stranded cDNA followed by directional cloning into a vector before RNA synthesis. Goller does not teach the addition of separate enzymes for synthesis of first and second-strand cDNA. Goller *et al.* also fails to teach the addition of a four-enzyme mix comprising a DNA polymerase for second-strand cDNA synthesis. In addition, the method of Goller *et al.* teaches the use of multiple tubes and organic extraction and precipitation. Applicants respectfully request reconsideration and withdrawal of the present rejection.

Obviousness Rejection Under 35 U.S.C. 103 - Sooknanan et al. in view of Schnipelsky et al.

Claims 20-21 were rejected under 35 U.S.C. § 103(a) over Sooknanan *et al.* as applied to claims 1 and 3-7 above, and further in view of Schnipelsky *et al.* (5,229,297). See, paper No. 17 at page 7, paragraph 10. Applicants respectfully traverse this rejection.

For the reasons indicated above, Sooknanan *et al.* fails to teach all of the limitations of claim 1 and Schnipelsky et al. fails to remedy the deficiencies of Sooknanan *et al.* as applied to dependent claims 20-21.

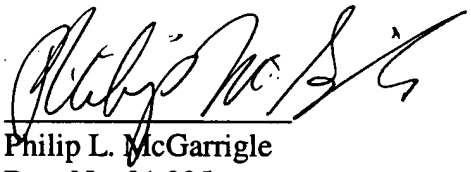
For these reasons and the reasons set forth *supra*, Applicants respectfully request that the rejection of claims under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

CONCLUSION

For the foregoing reasons, Applicants believe all the pending claims are now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5021.

Dated: January 10, 2001

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE TO THE APPLICATION

In the Claims:

Claims have been amended as follows:

1. A method for the amplification of a population of nucleic [acid] acids, said method comprising:

synthesizing double-stranded DNA from a single-stranded DNA population wherein a four-enzyme mix comprising a DNA polymerase is added to synthesize said double-stranded DNA, and

producing multiple copies of RNA from said double-stranded DNA,

wherein said amplification occurs in a single reaction vessel [comprising a four enzyme mix, and wherein said amplification is proportional].

25. The method of claim 1, wherein [said single-phase amplification comprises a] said four-enzyme mix further comprises [wherein said] enzymes [are] selected from the group consisting of DNA polymerase, RNA polymerase reverse transcriptase, terminal transferase, ligase and RNase.

26. (new) The method of claim 1 wherein the DNA polymerase is thermal-stable.